Aberrant beta-catenin distribution as potential prognosticator for endometrioid endometrial cancer recurrence

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Topic: Endometrial

Objectives
Aberrant beta-catenin distribution has been theorized as a predictive biomarker for recurrence in early stage, low grade endometrioid endometrial cancer.

Methods
This retrospective single institution cohort study reviewed 410 patients with endometrial cancer from May 2018 to May 2022. Uterine serous, carcinosarcoma, clear cell, de-differentiated, and mixed endometrial histology were excluded. Age at diagnosis, body mass index (BMI, kg/m2), race/ethnicity, FIGO 2009 cancer stage and grade, beta-catenin status by immunohistochemistry (aberrant nuclear distribution vs. wild-type plasma membrane distribution), recurrence status (locoregional vs. distant), lymphovascular space invasion (LVSI) and percent of myometrial invasion were obtained from the medical records. Tumor molecular characteristics including p53, mismatch repair (MMR), estrogen receptor (ER), progesterone receptor (PR) and POLE expression were collected. Stage was classified as early (stage IA/IB) or advanced (stage II/IIIA/IIIB/IIIC/IVB). X2 test, Fisher test, adjusted multivariable logistic regressions, sensitivity analyses for early stage/low grade and no specific molecular profile (NSMP) tumors were performed.

Results
298 patients were included. Most patients were White (58.7%), over 70 years old (33.2%), and obese (53.7%), with FIGO stage IA (55.4%) and grade 1 disease (65.8%). Nearly half of tumors were aberrant beta-catenin (45.3%) and almost 70% were MMR proficient. Almost all tumors were p53 wild type (94%), POLE wild type (95%), ER positive (98%), and PR positive (97.3%). Aberrant beta-catenin distribution was observed in 74.1% of FIGO grade 1 tumors, 22.5% of tumors with LVSI and in two-thirds of patients younger than 70 years old (68.8%). Recurrences were observed in 48 patients (16.1%) vs. no recurrences in 250 patients (83.9%). Recurrences did not correlate with beta catenin distribution: aberrant status was observed in 39.6% of recurrences vs. 46.4% without recurrence (p=0.38). Most recurrences occurred in the vagina (29.2%), followed by the lung (25%). Among the early stage (IA/IB), grade 1-2 cohort, recurrence did not vary significantly by beta-catenin status with 42.9% of aberrant status with recurrence versus 47.2% of aberrant status without recurrence (p=0.71). In the NSMP cohort, recurrence did not vary significantly by aberrant beta-catenin status (61.9% recurred vs. 53.2% did not recurred) (p=0.45). In adjusted logistic regression for age, BMI, race/ethnicity, stage, grade, LVSI and myometrial invasion, aberrant beta-catenin distribution did not affect disease recurrence in the overall cohort with aOR 0.53 [95% CI 0.11, 2.46]. Similar non-significant effect seen in the early stage/low grade cohort with aOR 1.09 [0.35-3.30], and the NSMP cohort with aOR 0.53 [0.11, 2.46]. For locoregional recurrence, p53 mutation had a four-fold risk with crude OR 4.58 [0.79-26.7] and POLE mutation did not have an increased risk with crude OR 0.84 [0.10-6.9]. Aberrant beta-catenin status did not have an effect on locoregional

recurrence with aOR 0.65 [0.15-2.85].

Conclusions

Aberrant beta-catenin distribution did not significantly correlate with recurrence in early stage, low grade endometrioid uterine cancer. We are currently further exploring the effect of aberrant beta-catenin distribution on endometrial cancer prognosis after adjuvant radiation.

Abstract Table or Graph

Aberrant nuclear beta-catenin staining does not result in increased odds of recurrence among patients with endometrioid endometrial cancer following surgical staging[1]

	Normal beta-catenin	Aberrant beta-catenin	Crude OR [95% CI]	Adjusted OR [95% CI] [2]
Recurrence	29/163 (17.8)	19/135 (14.1)	0.70[0.27, 1.78]	0.53[0.11, 2.46]
Locoregional recurrence	17/163 (10.4)	11/135 (8.1)	0.69[0.27, 1.75]	0.65[0.15, 2.85]
Recurrence in early-stage, low-grade disease	12/106 (6.0)	9/93 (9.7)	1.19[0.48, 3.97]	1.09[0.35, 3.30]
Recurrence in NSMP	8/21 (38.1)	13/21 (61.9)	0.70[0.27, 1.78]	0.53[0.11, 2.46]

[1] Data presented as number (column %)

[2] Adjusted by age, BMI, race, ethnicity, stage, grade, lympho-vascular invasion, myometrial involvement